REMARKS

The Invention

The present invention features methods and compositions for modifying the carbohydrate, lipid, and protein storage reserves of plants. The invention is based on Applicants' isolation and characterization of the SSE1 gene which, when inactivated, causes the shrunken seed phenotype.

Support for Claim Amendments

Support for the amendment to claim 8 is found, for example, in claim 9 (canceled herewith) and in the specification at page 2, lines 13-18 and page 24, lines 17-21. Support for the amendment to claim 21 is found, for example, in the specification at page 10, lines 11-19. Support for the amendment to claim 23 and new claim 40 is found, for example, in the specification at page 10, line 20 though page 11, line 11. No new matter is introduced by these amendments.

A "marked up" version of the claims showing the changes made and an appendix of the claims as pending are attached.

The Office Action

Claims 1, 3-13, and 15-26 are pending in this application. Claims 1, 3-13, and 15-26 stand rejected under 35 U.S.C. § 112, first paragraph, for both lack of enablement and inadequate written description. Claims 1, 3-13, and 15-26 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Claim 21 stands rejected under 35 U.S.C. § 102(b) as anticipated by Akama *et al.* (Plant Cell Reports, 12:7-11, 1992). Claims 8 and 11-12 stand rejected under 35 U.S.C. § 102(b) as anticipated by Storozhenko *et al.* (FEBS Lett., 390:113-118, 1996). Claims 23-26 stand rejected under 35 U.S.C. § 102(b) as anticipated by Lee *et al.* (Mol. Gen. Genet., 252:11-19, 1996). Claims 8, 10-13, 15-19, and 21-26 stand rejected under 35 U.S.C. § 103(a) as obvious over Lee *et al.* in view

of Storozhenko *et al.*

Drawing Objections

Applicants enclose herewith a set of substitute drawings. No new matter is introduced in these drawings.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-13 and 15-26 stand rejected under 35 U.S.C. § 112, first paragraph, for both lack of enablement and inadequate written description.

Enablement

Claims 1-13 and 15-22 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

Applicants respectfully note that the Patent Office has the initial burden to establish a reasonable basis to question enablement. In *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971), the court stated:

> a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

The MPEP (§ 2164.04) echoes the findings of Marzocchi:

> (I)t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the Appellant to go to the trouble and expense of supporting his presumptively accurate disclosure.

The rejection, in essence, is based on the assertion that "nucleic acids encoding

proteins with 30% identity to SEQ ID NO: 2 would encode proteins with many more than a single amino acid substitution ... nucleic acids with many substitutions would need to be made and analyzed." To address this issue, applicants note that the Federal Circuit has held that a large amount of experimentation does not necessarily constitute undue experimentation. For example, the *Wands* court (*In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404 (Fed. Cir. 1988)) stated that "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands* involved a method for identifying monoclonal antibodies that are specific for a particular antigen. The method required screening large numbers of hybridomas to determine which ones secrete an antibody with the desired characteristics. There was no question that the identification of a useful hybridoma line was a rare event and required substantial screening. The broad claim was held enabled nonetheless.

Applicants note that their specification provides several methods for screening candidate genes falling within the scope of the present claims; none of which require undue experimentation. For example, on page 16 and the results shown in Fig. 2B, applicants provide complementation screening assays. Further, extensive guidance is provided on methods for creating *Arabidopsis* transgenes and transfection constructs (pages 27-33), performing plant transformations (pages 33-35), and regenerating plants after transformation (pages 35-37). A functional screen, utilizing yeast *pex16* mutants, is also provided. Applicants, for example, have demonstrated that SSE polypeptides complement yeast *pex16* mutants as described at page 19, line 5, through page 20, line 20. Here, *Y. lipolytica* mutants, transfection constructs, and culture conditions are provided which allow for functional SSE polypeptide testing. Applicants experimental results describe a restoration of peroxisomal function and the complementation of mutants to grow on oleic acid as a sole carbon source.

Finally, applicants note that the Board of Patent Appeals and Interferences recently held a specification to be enabling for integration of a desired gene into fish embryos even though the methods described in the specification had a success rate of only 1%. *Ex parte Chen*, 61 U.S.P.Q.2d 1025 (Bd. Pat. App. & Int. 2000). The Board, appreciating the need for routine screening, noted that the 1% success rate "would reasonably appear to reflect the need for a repetitive procedure, rather than undue experimentation by those wishing to practice the invention." *Chen*, at 1028. Since the Patent Office, in this case, has not offered any evidence that the instantly claimed invention would require more than routine screening to practice, it has not carried its burden of showing a reasonable basis to doubt the enablement of the present claims. This basis of the rejection under § 112, first paragraph, for lack of enablement should, therefore, be withdrawn.

Claims 23-26, which are directed to vectors for producing antisense RNA and plants containing such vectors, remain rejected for lack of enablement. The Office Action points to several scientific publications as evidence that the effects of antisense expression are highly unpredictable. From this, it is concluded that undue experimentation would be required to practice the claimed invention. Applicants respectfully traverse this rejection.

As noted previously, it is improper to find that such experimentation is "undue" simply because some "trial and error" is necessary. *W.L. Gore & Assoc. V. Garlock, Inc.* 721 F.2d 1540, 1557, 220 U.S.P.Q. 303, 316 (Fed. Cir. 1983), even when the experimentation is needed to weed out inoperative embodiments. *Atlas Powder v. E.I. DuPont deNemours*, 750 F.2d 1569, 1576-77, 224 U.S.P.Q. 409, 414 (Fed. Cir. 1984).

The Office attempts to highlight the "unpredictability" by pointing to the seemingly disparate results of van der Krol *et al.* (Plant Mol. Biol. 14:457-466), Bird *et al.* (BioTechnol. 9: 635-639, 1991), Kuipers *et al.* (Mol. Gen. Genet. 246:745-755, 1995), Klann *et al.* (Plant Physiol. 112:1321-1330) and Tang *et al.* (Plant Cell 11:177-

189). These studies, however, successfully utilized antisense technology to reduce plant gene expression for a variety of genes in different plant species. These examples clearly demonstrate that it is routine in the art to screen large numbers of antisense transformants to identify those plants with desired characteristics.

The Office also points out that Colliver *et al.* (Plant Mol. Biol., 35:509-522, 1997) discovered increased chalcone synthase transcripts in *L. corniculatus* transformed with antisense constructs. Applicants once again point out that plants falling with the scope of applicants claims are obtained using routine screening. These methods were known to plant molecular biologists before the priority date of the present application, and such routine screening experiments do not constitute undue experimentation. This final basis of § 112 rejection should also be withdrawn.

Written Description

Claims 1-13 and 15-26 stand rejected, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to convey to one skilled in the art that the inventors had possession of the claimed invention. Applicants respectfully traverse this basis of the rejection.

To provide a description of an invention, applicants in their specification need only 'convey clearly to those skilled in the art to whom it is addressed...the information that [the inventor] has invented the specific subject matter later claimed.'" *Martin v. Mayer*, 823 F.2d 500, 505, 3 U.S.P.Q.2d 1333, 1337 (Fed. Cir. 1987). Applicants submit that they have satisfied this standard.

The specification and claims adequately describe the genus of SSE polypeptides claimed by Applicants. The claims, as presently amended, encompass nucleic acids encoding a polypeptide that is at least 30% identical to SEQ ID NO: 2, or hybridizes to SEQ ID NO: 1. As noted in Applicants' previous reply, the specification describes a hydrophoblic and a hydrophilic domain as well as several biological activities of an SSE

polypeptide. SSE biological activities include, for example, the ability to complement either the shrunken seed phenotype when introduced into an sse1 mutant (e.g., page 16, line 12, through page 12, line 22) or the *pex16* mutation in *Y. lipolytica* (page 19, line 20, through page 21, line 9). Thus, the specification clearly conveys to a skilled artisan that Applicants were in possession of the presently claimed invention. Applicants further submit that the specification provides an adequate written description of the nucleic acids as now claimed, and that its specification vis-a-vis the claims is in compliance with the Written Description Guidelines issued by the U.S. Patent and Trademark Office.

Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1, 3-13, and 15-26 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness.

Claims 1, 3-9, and 23 were deemed indefinite in reciting the term "SSE." This term has been removed from the claims, and this basis for the rejection is now moot.

Claim 8 was deemed indefinite for its recitation of "low stringency" because those hybridization conditions were not specified. Claim 8, as amended, now recites specific low stringency hybridization conditions, and this rejection should be withdrawn.

Rejections Under 35 U.S.C. § 102

Claim 21 stands rejected under 35 U.S.C. § 102(b) as anticipated by Akama *et al.* (Plant Cell Reports, 12:7-11, 1992). This claim has been amended according to the suggestions of the Examiner and this rejection may be withdrawn.

Claims 8 and 11-12 stand rejected under 35 U.S.C. § 102(b) as anticipated by Storozhenko *et al.* (FEBS Lett., 390:113-118, 1996). As amended, these claims now require isolating a polypeptide having at least 30% identity to the amino acid sequence depicted in SEQ ID NO:2, subject matter which has been deemed by the Office to be

"free of the prior art." Accordingly, this basis of the § 102 rejection should be withdrawn.

Claims 23-26 stand rejected under 35 U.S.C. § 102(b) as anticipated by Lee *et al.* (Mol. Gen. Genet., 252:11-19, 1996). As amended, these claims now require an expression vector that includes an isolated DNA molecule encoding antisense RNA based on a nucleic acid encoding a polypeptide having at least 30% identity to the amino acid sequence shown in Fig. 2B (SEQ ID NO:2). This final basis of the § 102 rejection, in view of this amendment, should be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Claims 8, 10-13, 15-19, and 21-26 stand rejected under 35 U.S.C. 103(a) over Lee *et al.* (*supra*), in view of Storozhenko *et al.* (*supra*). As is discussed above, these claims are now directed to subject matter that has been deemed to be free of the prior art, and this rejection may be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is requested. Enclosed is a petition to extend the period for replying for three months, to and including November 21, 2002. Also enclosed is a Notice of Appeal to the Board of Patent Appeals and Interferences.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Applicants respectfully request that, effective immediately, all communication in this case be addressed to:

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Respectfully submitted,

Date: 21 November 2002

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\\Clark-w2k1\documents\00786\368xxx\00786.368002 Reply to OA mailed 5.21.02.wpd

Version With Markings to Show Changes Made

1. (Twice Amended) An isolated nucleic acid molecule comprising a sequence encoding [an SSE] a polypeptide having at least 30% identity with the amino acid sequence shown in Fig. 2B (SEQ ID NO: 2).

3. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes [an SSE] a polypeptide that, when expressed in a cell of a plant, modifies the production of food storage reserves.

4. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes [an SSE] a polypeptide that, when expressed in a cell of a plant, facilitates the intracellular transport of a storage protein.

5. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes [an SSE] a polypeptide that, when expressed in a cell of a plant, facilitates the formation of protein bodies.

6. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes [an SSE] a polypeptide that, when expressed in a cell of a plant, facilitates the formation of oil bodies.

8. (Twice Amended) An isolated nucleic acid molecule comprising a sequence encoding [an SSE] a polypeptide having at least 30% sequence identity to SEQ ID NO: 2, wherein said isolated nucleic acid molecule hybridizes under low stringency conditions to the nucleic acid molecule comprising the cDNA of Fig. 2A (SEQ ID NO:1), wherein said low stringency conditions comprise:

(i) hybridization at about 42°C, 40% formamide, 0.1 mg/ml sheared salmon sperm

DNA, 0.5% SDS, 5X SSPE, and 1X Denhardt's reagent;

(ii) two washes at room temperature, 2X SSC, and 0.1% SDS; and

(iii) two washes at room temperature, 0.5X SSC, and 0.1% SDS.

21. (Amended) A seed [from a transgenic plant or transgenic plant component of claim 16] comprising the isolated nucleic acid of claim 1 or 8.

23. (Amended) An expression vector comprising an isolated DNA molecule encoding antisense RNA based on a nucleic acid encoding a polypeptide having at least 30% identity to the amino acid sequence shown in Fig. 2B (SEQ ID NO:2) [for producing antisense SSE RNA].

Claims as Pending

1. (Twice Amended) An isolated nucleic acid molecule comprising a sequence encoding a polypeptide having at least 30% identity with the amino acid sequence shown in Fig. 2B (SEQ ID NO: 2).

3. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes a polypeptide that, when expressed in a cell of a plant, modifies the production of food storage reserves.

4. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes a polypeptide that, when expressed in a cell of a plant, facilitates the intracellular transport of a storage protein.

5. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes a polypeptide that, when expressed in a cell of a plant, facilitates the formation of protein bodies.

6. (Amended) The nucleic acid molecule of claim 1, wherein said sequence encodes a polypeptide that, when expressed in a cell of a plant, facilitates the formation of oil bodies.

7. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is cDNA.

8. (Twice Amended) An isolated nucleic acid molecule comprising a sequence encoding a polypeptide having at least 30% sequence identity to SEQ ID NO: 2, wherein said isolated nucleic acid molecule hybridizes under low stringency conditions to the

nucleic acid molecule comprising the cDNA of Fig. 2A (SEQ ID NO:1), wherein said low stringency conditions comprise:

(i) hybridization at about 42°C, 40% formamide, 0.1 mg/ml sheared salmon sperm DNA, 0.5% SDS, 5X SSPE, and 1X Denhardt's reagent;

(ii) two washes at room temperature, 2X SSC, and 0.1% SDS; and

(iii) two washes at room temperature, 0.5X SSC, and 0.1% SDS.

10. The isolated nucleic acid molecule of claim 1 or 8, wherein said nucleic acid molecule is operably linked to a promoter functional in a plant cell.

11. An expression vector comprising the nucleic acid molecule of claim 1 or 8, said vector being capable of directing expression of the polypeptide encoded by said nucleic acid molecule.

12. (Amended) A cell transformed with the isolated nucleic acid molecule of claim 1 or 8.

13. The cell of claim 12, wherein said cell is a plant cell.

15. The cell of claim 12, wherein said bacterial cell is *Agrobacterium*.

16. (Amended) A plant or plant component transformed with a nucleic acid molecule of claim 1 or 8, wherein said nucleic acid molecule is expressed in said plant or said plant component.

17. The plant or plant component of claim 16, wherein said transgenic plant or transgenic plant component is an angiosperm.

18. The plant or plant component of claim 16, wherein said transgenic plant or transgenic plant component is a dicot.

19. The plant or plant component of claim 16, wherein said transgenic plant or transgenic plant component is a cruciferous plant.

20. The plant or plant component of claim 16, wherein said transgenic plant or transgenic plant component is a monocot.

21. (Amended) A seed comprising the isolated nucleic acid of claim 1 or 8.

22. A cell from a transgenic plant or transgenic plant component of claim 16.

23. (Amended) An expression vector comprising an isolated DNA molecule encoding antisense RNA based on a nucleic acid encoding a polypeptide having at least 30% identity to the amino acid sequence shown in Fig. 2B (SEQ ID NO:2).

24. A transgenic plant or transgenic plant component comprising the vector of claim 23.

25. A seed from a transgenic plant or transgenic plant component of claim 24.

26. A cell from a transgenic plant or transgenic plant component of claim 24.